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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/559,676	12/07/2005	Judith A. Boice	21294P	1543

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EXAMINER	
CLARK, SARA E	
ART UNIT	PAPER NUMBER
1612	
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07/07/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/559,676	BOICE ET AL.	
	Examiner	Art Unit	
	SARA E. CLARK	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-11,16 and 22-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2, 4-11, 16, and 22-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/14/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

FINAL REJECTION

Receipt is acknowledged of Applicants' Amendments and Remarks, filed 4/15/2010.

Claims 3, 12, 14, 15, 17, 19, and 21 have been cancelled.

Claims 13, 18, and 20 stand withdrawn as drawn to nonelected species.

Claim 1 has been amended.

No new claims have been added.

Thus, claims 1, 2, 4-11, 16, and 22-26 now represent all claims currently pending and under consideration.

INFORMATION DISCLOSURE STATEMENT

The information disclosure statement (IDS) submitted on 4/14/2010 was filed after the mailing date of the non-final Office Action on 1/15/2010. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

WITHDRAWN REJECTIONS

Rejections under 35 USC §112, First Paragraph

Due to the amendments to the claims, the rejection of claims 1-6, 8-11, 16, and 22-26 under 35 USC 112, first paragraph, for lack of an enabling disclosure with respect to the term "preventing," is withdrawn.

Rejections under 35 USC §102(e)

Due to the amendments to the claims, the rejection of claims 1-11, 16, and 24-26 under 35 USC 102(e) as anticipated by DiSalle (WO02/72106), is withdrawn.

Rejections under 35 USC §103

Due to the amendments to the claims, the rejection of claims 1-11 and 16 under 35 USC 103 as obvious over Masferrer and Riendeau is withdrawn.

Due to the amendments to the claims, the rejection of claims 1, 22, 23, 25, and 26 under 35 USC 103 as obvious over DiSalle and Heinrichs is withdrawn.

MAINTAINED REJECTIONS

The following rejection made in the Office Action dated 1/15/2010 is maintained on the grounds that it continues to read on the amended claims.

Rejections under 35 USC §112, First Paragraph

Claim 7 stands rejected under 35 USC 112, first paragraph, for lack of an enabling disclosure with respect to the term "preventing."

NEW REJECTIONS

Claim Rejections - 35 USC § 112, First Paragraph

New Matter

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 1, 2, 4-11, 16, and 22-26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

Specifically, amended claim 1 is drawn to a method of treating endometriosis consisting of the administration of an effective amount of a cyclooxygenase-2 selective inhibitor selected from the group consisting of rofecoxib, etoricoxib, celecoxib, valdecoxib, lumiracoxib, BMS347070, tiracoxib, ABT963, CS502, and GW406381.

The disclosure does not support the limitation "consisting of," which is a transitional phrase excluding any element, step, or ingredient not specified in the claim (see MPEP §2111.03). For example, the specification (page 8, lines 28-32) discloses that the active agents are typically administered in admixture with suitable diluents, excipients or carriers, and Examples 1-6 set forth formulations containing a COX-2 inhibitor in combination with pharmaceutical excipients. However, the transitional phrase "consisting of" limits the claims to only the components which are positively recited in

the claims, and thus excludes excipients.

Therefore, an amendment limiting the scope of the claim from "comprising" to "consisting of" excludes subject matter previously encompassed by the claims. Any negative claim limitation or exclusionary proviso must have basis in the original disclosure (see MPEP §2173.05(i)). Further, as recognized by MPEP §706.03(o), "[n]ew matter includes not only the addition of wholly unsupported subject matter, but may also include adding specific percentages or compounds after a broader original disclosure, or even the omission of a step from a method." See MPEP § 608.04 to § 608.04(c).

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

4. Claims 1, 2, 4-11, 16, and 24 are rejected under 35 U.S.C. 102(e) as being anticipated by Visser et al. (WO03/17973, provided by Applicant on the IDS dated 4/14/2010).

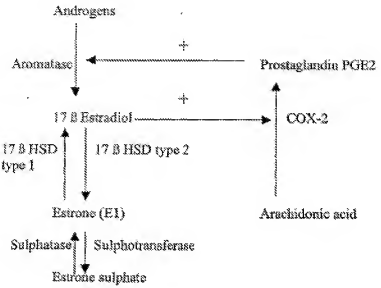
Visser et al. disclose methods of treating endometriosis by administering a

selective estrogen enzyme modulator (SEEM) consisting of a cyclooxygenase 2 (COX-2) selective inhibitor (abstract). The elected compound, etoricoxib, is disclosed as a suitable COX-2 selective inhibitor (p. 9, line 6; p. 11, line 12), as recited by claim 16.

The methods of Visser et al. include treatment of endometriosis resulting in resolution of the endometriotic tissue (p. 4, lines 12-13), as well as prophylactic treatment (p. 10, line 14). Administration of the SEEM leads to a reduction in proliferation of endometriotic lesions and inhibition of the growth of endometriotic tissues, so that they do not increase in volume, no new such tissues are formed, and existing lesions atrophy or are fully eliminated (p. 11, line 32 to p. 12, line 5). This implicitly discloses retarding the development of endometriotic lesions, as recited by claims 2 and 6; reversing the development of endometriotic lesions, as recited by claims 4 and 8; reducing the number or severity of endometriotic lesions, as recited by claim 5; and preventing the development of endometriotic lesions, as recited by claim 7, encompassing the patient population recited by claims 1, 2, 4-11, and 16.

Visser et al. disclose that inhibition of COX-2 will automatically cause a reduction of aromatase activity, i.e., inhibiting aromatase (p. 7, lines 37-39), as recited by claim 9. This implicitly results in a reduction in elevated levels of aromatase, as recited by claims 10 and 11.

In addition, Visser et al. disclose that the two common treatments for endometriosis are surgery or hormonal therapy, or a combination of both. Because COX-2 inhibitors are disclosed to interfere with endogenous estradiol synthesis (see figure on p. 7),



Visser et al. implicitly disclose the perioperative administration of the disclosed COX-2 inhibitors in conjunction with or as a follow-up to surgical removal of implants, as recited by claim 24.

Thus, Visser et al. anticipates claims 1, 2, 4-11, 16, and 24.

5. Claims 1, 2, and 4-11 are rejected under 35 U.S.C. 102(e) as being anticipated by Jabbour (US Pub. 2003/0100591, provided by Applicant on the IDS dated 4/14/2010).

Jabbour discloses methods of treating or preventing pathological conditions of the uterus by administering a COX-2 selective inhibitor (abstract), to include endometriosis and fibroids (paras. 0002, 0008). VIOXX (rofecoxib, see attached) is disclosed as a suitable COX-2 selective inhibitor, as recited by claims 1, 2, and 4-11. Jabbour discloses that the COX-2 selective inhibitor is administered in an effective

amount to combat the undesired pathological condition of the uterus. Thus, the compound may be used to alleviate symptoms (palliatively), to treat the condition, or administered prophylactically to prevent the condition, at a dose which produces a beneficial therapeutic effect in the patient (para. 0051).

Thus, Jabbour implicitly and/or inherently discloses the treatment of endometriosis by administering a COX-2 selective inhibitor in a manner which retards the development of endometriotic lesions, as recited by claims 2 and 6; reversing the development of endometriotic lesions, as recited by claims 4 and 8; reducing the number or severity of endometriotic lesions, as recited by claim 5; and preventing the development of endometriotic lesions, as recited by claim 7, and encompasses the patient population recited by claims 1, 2, and 4-11. See MPEP §2112.

Thus, Jabbour anticipates claims 1, 2, and 4-11.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. Claims 1, 2, 4-11, 16, and 22-26 rejected under 35 U.S.C. 103(a) as being unpatentable over Visser et al. (WO03/17973).

As discussed above, Visser et al. disclose methods of treating endometriosis by

administering a selective estrogen enzyme modulator (SEEM) consisting of a cyclooxygenase 2 (COX-2) selective inhibitor (abstract). The elected compound, etoricoxib, is disclosed as a suitable COX-2 selective inhibitor (p. 9, line 6; p. 11, line 12), as recited by claim 16.

The methods of Visser et al. include treatment of endometriosis resulting in resolution of the endometriotic tissue (p. 4, lines 12-13), as well as prophylactic treatment (p. 10, line 14). Administration of the SEEM leads to a reduction in proliferation of endometriotic lesions and inhibition of the growth of endometriotic tissues, so that they do not increase in volume, no new such tissues are formed, and existing lesions atrophy or are fully eliminated (p. 11, line 32 to p. 12, line 5). This implicitly discloses retarding the development of endometriotic lesions, as recited by claims 2 and 6; reversing the development of endometriotic lesions, as recited by claims 4 and 8; reducing the number or severity of endometriotic lesions, as recited by claim 5; and preventing the development of endometriotic lesions, as recited by claim 7, encompassing the patient population recited by claims 1, 2, 4-11, and 16.

Visser et al. disclose that inhibition of COX-2 will automatically cause a reduction of aromatase activity, i.e., inhibiting aromatase (p. 7, lines 37-39), as recited by claim 9. This implicitly results in a reduction in elevated levels of aromatase, as recited by claims 10 and 11.

In addition, Visser et al. disclose that the two common treatments for

endometriosis are surgery or hormonal therapy, or a combination of both. Because COX-2 inhibitors are disclosed to interfere with endogenous estradiol synthesis (see figure on p. 7).

Visser et al. implicitly disclose the perioperative administration of the disclosed COX-2 inhibitors in conjunction with or as a follow-up to surgical removal of endometriotic implants, as recited by claim 24.

Visser et al. also disclose that oral contraceptives are administered to treat endometriosis (p. 5, lines 4-5), as recited by claim 22. In particular, the progestogens medroxyprogesterone acetate and lynestrenol were known to be administered to treat endometriosis (p. 4, lines 29-34), as recited by claims 23. Visser et al. further disclose that GnRH agonists have been used to treat endometriosis (p. 4, lines 25-26), such as nafareline and busereline (p. 2, line 32), as recited by claim 25. Nafarelin(e) and buserelin(e) and typically administered as the acetate salts (see attached), as recited by claim 26.

While Visser et al. teach that certain drawbacks can be associated with the administration of GnRH agonists, progestogens, and oral contraceptives (see pp. 4-5), the independent utility of COX-2 selective inhibitors, GnRH agonists, and medroxy-progesterone acetate and lynestrenol in the treatment of endometriosis is nonetheless disclosed. Thus, it would have been *prima facie* obvious to a skilled artisan at the time the invention was made to concomitantly or sequentially co-administer a COX-2 selective inhibitor with the oral contraceptives medroxy-progesterone acetate or lynestrenol, as recited by claims 22 and 23, or with the GnRH agonists nafarelin acetate

or buserelin acetate, as recited by claims 25 and 26, with a reasonable expectation of success.

As recognized by MPEP §2144.06, "it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

8. Claims 1, 2, 4-11, 16, and 22-26 rejected under 35 U.S.C. 103(a) as being unpatentable over Visser et al. (WO03/17973) in view of Heinrichs (USPN 6,265,393).

As discussed above, Visser et al. disclose methods of treating endometriosis by administering a selective estrogen enzyme modulator (SEEM) consisting of a cyclooxygenase 2 (COX-2) selective inhibitor (abstract). The elected compound, etoricoxib, is disclosed as a suitable COX-2 selective inhibitor (p. 9, line 6; p. 11, line 12), as recited by claim 16.

The methods of Visser et al. include treatment of endometriosis resulting in resolution of the endometriotic tissue (p. 4, lines 12-13), as well as prophylactic treatment (p. 10, line 14). Administration of the SEEM leads to a reduction in proliferation of endometriotic lesions and inhibition of the growth of endometriotic tissues, so that they do not increase in volume, no new such tissues are formed, and existing lesions atrophy or are fully eliminated (p. 11, line 32 to p. 12, line 5). This

implicitly discloses retarding the development of endometriotic lesions, as recited by claims 2 and 6; reversing the development of endometriotic lesions, as recited by claims 4 and 8; reducing the number or severity of endometriotic lesions, as recited by claim 5; and preventing the development of endometriotic lesions, as recited by claim 7, encompassing the patient population recited by claims 1, 2, 4-11, and 16.

Visser et al. disclose that inhibition of COX-2 will automatically cause a reduction of aromatase activity, i.e., inhibiting aromatase (p. 7, lines 37-39), as recited by claim 9. This implicitly results in a reduction in elevated levels of aromatase, as recited by claims 10 and 11.

In addition, Visser et al. disclose that the two common treatments for endometriosis are surgery or hormonal therapy, or a combination of both. Because COX-2 inhibitors are disclosed to interfere with endogenous estradiol synthesis (see figure on p. 7).

Visser et al. implicitly disclose the perioperative administration of the disclosed COX-2 inhibitors in conjunction with or as a follow-up to surgical removal of endometriotic implants, as recited by claim 24.

Visser et al. also disclose that oral contraceptives are administered to treat endometriosis (p. 5, lines 4-5), as recited by claim 22. In particular, the progestogens medroxyprogesterone acetate and lynestrenol were known to be administered to treat endometriosis (p. 4, lines 29-34), as recited by claims 23. Visser et al. further disclose that GnRH agonists have been used to treat endometriosis (p. 4, lines 25-26), such as nafareline and busereline (p. 2, line 32), as recited by claim 25. Nafarelin(e) and

buserelin(e) and typically administered as the acetate salts (see attached), as recited by claim 26.

While Visser et al. teach that certain drawbacks can be associated with the administration of GnRH agonists, progestogens, and oral contraceptives (see pp. 4-5), the independent utility of COX-2 selective inhibitors, GnRH agonists, and medroxy-progesterone acetate and lynestrenol in the treatment of endometriosis is nonetheless disclosed. Thus, it would have been *prima facie* obvious to a skilled artisan at the time the invention was made to concomitantly or sequentially co-administer a COX-2 selective inhibitor with the oral contraceptives medroxy-progesterone acetate or lynestrenol, as recited by claims 22 and 23, or with the GnRH agonists nafarelin acetate or buserelin acetate, as recited by claims 25 and 26, with a reasonable expectation of success.

In addition, Heinrichs discloses methods of treating symptoms of endometriosis, as well as prophylactic treatment to prevent their recurrence (col. 4, lines 15-33), by the administration of a GnRH agonist, to include leuprolide acetate (col. 9, lines 30-35), followed by the co-administration of an estrogen agent and a progestin agent such as norethindrone. (col. 8, lines 30-45; Table 2).

Thus, on the basis of the teachings Heinrichs, it would have been predictable to a skilled artisan that endometriosis could be treated or prevented by co-administering the COX-2 inhibitor etoricoxib, as taught by Visser et al., with the GnRH agonist leuprolide acetate and the progestin (oral contraceptive) norethindrone as taught by Heinrichs, because each of these agents was known to be effective independently. As recognized

by MPEP §2144.06, "it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose .... [T]he idea of combining them flows logically from their having been individually taught in the prior art." *In re Kerkhoven*, 626 F.2d 846,850, 205 USPQ 1069, 1072 (CCPA 1980).

Further, as recognized by MPEP §2143, combining prior art elements according to known methods to yield predictable results would motivate the skilled artisan to modify the references with a reasonable expectation of success. The rationale to support a conclusion of *prima facie* obviousness is that all the claimed elements were known in the prior art, and a skilled artisan could have combined the elements as claimed by known methods with no change in their respective functions, and the combination yielded nothing more than predictable results to one of ordinary skill in the art. See KSR Int'l Co. v. Teleflex Inc. (550 U .S. 398, 409).

RESPONSE TO ARGUMENTS

Applicant contends that because the disclosure of Heinrichs is directed to treatment and prevention of *signs and symptoms* of endometriosis, rather than *endometriosis itself*, the reference is not in the Applicant's field of endeavor, is not relevant to the subject matter of claims 1, 22, 23, 25, and 26, and therefore is not prior art (Remarks dated 4/15/2010, p. 10). This is not found persuasive for the following reasons.

First, Applicant makes the conclusory assertion that endometriosis, versus endometriosis signs and symptoms, are different diseases or disorders, while providing no supporting evidence, or explaining how the methods of Heinrichs would not treat endometriosis *per se*. In the absence of evidence to the contrary, treating the signs and symptoms of endometriosis in the manner taught by Heinrichs would inherently result in the treatment of endometriosis itself. See MPEP §2112.

Second, Visser et al, the primary reference, discloses the treatment and prevention of endometriosis; Heinrichs is cited as evidence that it would have been predictable to a skilled artisan to modify the methods of Visser et al. by co-administering an additional therapeutic agent, specifically the GnRH agonist leuprolide acetate or the oral contraceptive norethindrone.

Finally, in response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

CONCLUSION

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

CORRESPONDENCE

Any inquiry concerning this communication or earlier communications from the examiner should be directed to SARA E. CLARK whose telephone number is (571) 270-7672. The examiner can normally be reached on Mon - Thu, 7:30 am - 5:00 pm (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick Krass, can be reached on 571-272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/SARA E. CLARK/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612